New bis-Pyridinium Diquaternary Salts with Antimicrobial Properties

BIANCA FURDUI*, OANA CONSTANTIN†, AUREL TABACARU*, RODICA MIHAELA DINICA*

1"Dunărea de Jos" University of Galați, Faculty of Science and Environment, 111 Domneasca Str., 800201, Galați, Romania
2"Dunărea de Jos" University of Galați, Faculty of Food and Science Engineering, 47 Domneasca Str., 800008, Galați, Romania
3Università Degli Studi di Camerino, Dipartimento di Scienze Chimiche, Via S. Agostino 1, MC 62032 Camerino, Italy

The synthesis of a new series of asymmetric bis-pyridinium diquaternary salts using a N-alkylation reaction of 1,2-bis(4-pyridyl)ethane with reactive halides is reported. The structures of the salts were fully characterized by IR, NMR and mass spectroscopy and elemental analysis. Their antimicrobial activity against food spoilage microorganisms was comparatively investigated. Some of these compounds were found to inhibit the growth of microorganisms (bacteria and fungus) in function of structure and doses. The thermal stability of all species was also determined by thermogravimetric analysis.

Keywords: pyridinium quaternary salts, antimicrobial activity, TGA analysis

N-Heterocyclic quaternary ammonium salts such as pyridinium and bis-pyridinium salts are versatile classes of compounds having a wide range of interesting properties useful for biological and industrial applications and continuing to receive an increasing attention. Thus, the pyridinium salts attract the attention of scientists because they can be employed as electrochromic materials [1], cardiovascular, hypotensive and neuromuscular agents [2-3], as phase transfer agents and catalyst [4], acylating agents [5], initiators of cationic polymerization [6, 7], enzyme inhibitors [8], dyes, cationic surfactants [9] or ionic liquids [10], precursors of indolizine compounds by dipolar cycloaddition [11-13]. Moreover, pyridinium and bispyridinium quaternary salts represent an important group of chemicals widely used as biocides [14-16], drugs [17, 18] and herbicides [19, 20] due to their strong antimicrobial effect even at very small concentrations, on a broad range of gram-positive and gram-negative bacteria (i.e. Bacillus subtilis, Sarcina lutea, Streptococcus pneumoniae, Staphylococcus aureus, Micrococcus luteus, Escherichia coli etc.) and on some moulds species (Aspergillus niger, Aspergillus glaucus, Geotrichum candidum, Fusarium graminearum etc.) and yeasts (Saccharomyces cerevisiae, Rhodoturula glutinis etc.) [21-23].

The continuous increase of bacterial resistance to many antibiotic agents has limited the use of commercial disinfectants and imposed the necessity of a permanent identification of new compounds with microbiostatic and microbicidal effect. Past studies of our group include the development of nitrogen quaternary salts in particular antimicrobial agents with possible applicability in food industry disinfection processes, in the present study we have synthesized and characterized a new series of asymmetric diquaternary bis-pyridinium salts, based on the 1,2-bis(4-pyridyl)ethane. Their antimicrobial potential against food spoilage microorganisms (bacteria and fungus) and their thermal stability were also investigated.

Experimental part

Reagents used for synthesis were purchased from Aldrich, Fluka, and Merck companies. Organic solvents were purchased from Merck Company. Melting points were recorded with a Büchi Melting Point B-540. 1H NMR and 13C NMR spectra were recorded with a Bruker 400 Ultrashield (400MHz) spectrometer operating at room temperature. Deuterated DMSO was used as solvent. Abbreviations for data quoted are: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; m, multiplet. IR spectra were recorded from 4000 to 650 cm⁻¹ with a Perkin-Elmer Spectrum 100 instrument by total reflectance on a CdSe crystal. The electrospray ionization (ESI) mass spectra were measured on Thermo Scientific LC/MSQ Plus. Elemental analyses (C, H, N) were performed with a Fisons Instruments 1108 CHNS-O elemental analyzer. Melting points were recorded with an SMP3 Stuart instrument mounting a capillary apparatus. Thermogravimetric analyses (TGA) were carried out in a N₂ stream with a Perkin-Elmer STA 6000 simultaneous thermal analyzer, in thermal range of 30-500°C with heating rates of 7°C/min.

Synthesis

Preparation of N-methyl-1,2-bis-(4-pyridinium) ethane iodide (I). 1 g (5.4 mmol) 1,2-bis(4-pyridyl)ethane and 0.76g (5.3mmol; 0,33mL) methyl iodide were stirred at room temperature in acetonitrile (10mL) for 10 h. The solvent was removed by filtration and the obtained solid was washed with acetone and ethyl ether. Salt I is obtained as white-beige crystals, yield 47%; m.p. 180-181°C.

IR (ATR, cm⁻¹): 3011; 2960; 1640; 1601; 1574; 1557; 1517; 1471; 1414; 1185; 991. 1H NMR (400MHz, DMSO-d₆) δ/ppm: 8.84 (d, J = 6.4 Hz, 2H), 8.44 (dd, J = 4.46, 1.70 Hz, 2H), 7.74 (d, J = 6.4 Hz, 2H), 7.08 (dd, J =4.46, 1.70 Hz, 2H), 4.32 (s, 3H: N +CH₃); 3.43 (s, 4H: 2CH₂). 13C NMR (75 MHz, DMSO-d₆) δ ppm: 149.12 (C); 149.04 (C); 148.74 (2CH); 143.21 (2C); 140.82 (C); 125.96 (2C); 124.31 (2C); 46.36 (CH₃); 35.53 (2CH₂). MS (ESI+), m/z: 198 [M⁺-H⁺]. Anal. Calcd. for C₄₂H₂₂I₂N₄: C, 47.87; H, 4.64; N, 8.59. Found: C, 47.08; H, 4.46; N, 8.35.

* email: bturdui@ugal.ro, rodonica@ugal.ro; 0336 130 251
Preparation of α-iodo-acetophenones (2a-d), general procedure. 30 mmol bromo or chloro derivatives dissolved in 30 mL anhydrous acetonitrile were treated with 42 mmol (excess 40%) NAl dissolved in 30 mL anhydrous acetonitrile. The mixture was stirred for 30 min. at room temperature. While precipitate of formed NaBr or NaCl was removed by filtration. From the filtrate the solvent was evaporated and the oil residue was dissolved in chloroform. If it is necessary, the excess of NaBr or NaCl are removed by filtration of chloroformic solutions. Chloroform evaporation lead to desired products, with a high purity degree.

2-iodo-acetophenone (2a); yellow-red crystals with very low m.p.; yield 99%. 1H NMR (400 MHz, DMSO-d6) δ/ppm: 10.05 (s, 1H: OH); 9.43 (s, 1H: OOH); 7.42 (dd, J = 8.3 Hz, 2.2Hz, 1H), 7.36 (J = 2.2Hz, 1H); 6.81 (d, J = 8.3 Hz, 1H), 4.42 (s, 2H: CH2).

2-iodo-3',4'-dihydroxy-acetophenone (2b); beige-green crystals with low m.p.; yield 83%. 1H NMR (400 MHz, DCDCl3) δ/ppm: 7.96-7.99 (m, 2H), 7.58 (t, J = 7.39 Hz, 1H), 7.47 (t, J = 7.44 Hz, 2H), 4.35 (s, 2H: CH2).

IR (ATR, cm −1): 3008; 2957; 1691; 1639; 1594, 1578, 1521, 1494, 1462; 1345; 1284, 1246, 1174, 1139, 1032; 852, 759, 682, 631 cm−1.

2-iodo-4'-nitro-acetophenone (2c); yellow-beige crystals with low m.p.; yield 93%. 1H NMR (400 MHz, DCDCl3) δ/ppm: 8.34 (d, J = 9.0 Hz, 2H), 8.15 (d, J = 9.0 Hz, 2H), 4.39 (s, 2H: CH2).

IR (ATR, cm−1): 3034; 2933; 2907; 2835; 1618; 1639; 1575, 1519, 1511, 1246, 1032; 1175; 988. 1H NMR (400 MHz, DMSO-d6) δ/ppm: 8.94 (d, J = 6.8 Hz, 2H), 8.21 (d, J = 6.8 Hz, 2H), 8.11 (d, J = 6.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.37 (s, 2H: CH2), 4.32 (s, 3H: N+CH3), 4.22 (s, 3H: OCH3). MS (ESI+), m/z: 526 [M+H]+. Anal. Calcd. for C21H20I2N2O3 (Mr=604.22 g/mol): C, 44.08, H, 3.88, N, 4.90. Found: C, 44.28; H, 3.76; N, 4.85.

2-iodo-4'-metoxi-acetofenonei (2d); yellow crystals with low m.p.; yield 99%. 1H NMR (400MHz, DMSO-d6) δ/ppm: 8.94 (d, J = 6.4 Hz, 2H), 8.05 (d, J = 6.8 Hz, 2H), 8.15 (d, J = 6.8 Hz, 2H), 7.47 (t, J = 7.44 Hz, 2H), 4.42 (s, 2H: CH2), 3.48 (s, 3H: OCH3).

Preparation of asymmetric diquaternary salts of 1,2-bis-(4-pyridyl)ethane (3a-d), general procedure. Compound 1 (1 mmol) and reactive iodo derivatives (iodoacetophenones 2a-d, 1.50 mmol) were suspended in acetonitrile (10 mL). The mixture was heated at reflux, under vigorous stirring, for 15-20 h. The reaction product was separated by filtration of the hot reaction mixture, was washed with boiling acetonitrile and dried under vacuum at room temperature. The obtained compounds have a high purity level and do not necessitate further purification.

N-methyl-N'-(para-methoxy-phenacyl)-1,2-bis-(4-pyridinium)ethane diiodide (3a); yellow crystals, yield 70%; m.p. 210-211°C. IR (ATR, cm−1): 3008; 2957; 1519, 1511, 1246, 1188; 988. 1H NMR (400 MHz, DMSO-d6) δ/ppm: 8.94 (d, J = 6.8 Hz, 2H), 8.90 (d, J = 6.8 Hz, 2H), 8.21 (d, J = 6.8 Hz, 2H), 8.11 (d, J = 6.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.37 (s, 2H: CH2), 4.32 (s, 3H: N+CH3), 4.22 (s, 3H: OCH3). MS (ESI+), m/z: 526 [M+H]+. Anal. Calcd. for C21H20I2N2O3 (Mr=604.22 g/mol): C, 44.08, H, 3.88, N, 4.90. Found: C, 44.28; H, 3.76; N, 4.85.

Preparation of asymmetric diquaternary salts of 1,2-bis-(4-pyridyl)ethane (3a-d), general procedure. Compound 1 (1 mmol) and reactive iodo derivatives (iodoacetophenones 2a-d, 1.50 mmol) were suspended in acetonitrile (10 mL). The mixture was heated at reflux, under vigorous stirring, for 15-20 h. The reaction product was separated by filtration of the hot reaction mixture, was washed with boiling acetonitrile and dried under vacuum at room temperature. The obtained compounds have a high purity level and do not necessitate further purification.

N-methyl-N'-(para-nitro-phenacyl)-1,2-bis-(4-pyridinium)ethane diiodide (3b); yellow crystals, yield 68%; m.p. 255-256°C. IR (ATR, cm−1): 3034; 2933, 2907; 2835; 1618; 1639; 1575, 1519, 1511, 1246, 1032; 1175; 988. 1H NMR (400 MHz, DMSO-d6) δ/ppm: 8.94 (d, J = 6.8 Hz, 2H), 8.21 (d, J = 6.8 Hz, 2H), 8.11 (d, J = 6.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 2H), 7.21 (d, J = 8.8 Hz, 2H), 6.37 (s, 2H: CH2), 4.32 (s, 3H: N+CH3), 4.22 (s, 3H: OCH3). MS (ESI+), m/z: 526 [M+H]+. Anal. Calcd. for C21H20I2N2O3 (Mr=604.22 g/mol): C, 44.08, H, 3.88, N, 4.90. Found: C, 44.28; H, 3.76; N, 4.85.

Preparation of asymmetric diquaternary salts of 1,2-bis-(4-pyridyl)ethane (3a-d), general procedure. Compound 1 (1 mmol) and reactive iodo derivatives (iodoacetophenones 2a-d, 1.50 mmol) were suspended in acetonitrile (10 mL). The mixture was heated at reflux, under vigorous stirring, for 15-20 h. The reaction product was separated by filtration of the hot reaction mixture, was washed with boiling acetonitrile and dried under vacuum at room temperature. The obtained compounds have a high purity level and do not necessitate further purification.

Antimicrobial activity
The antimicrobial potential of the four asymmetric diquaternary salts derived from 1,2-bis-(4-pyridinium)-ethane 3a-d was investigated. The experimental protocol was similar with those previously applied by us for the investigation of antimicrobial activity of another symmetrical diquaternary salts derived 1,2-bis-(4-pyridinium)ethane [26].

Ten microorganism strains were used as test microorganisms for the evaluation of the inhibitory potential of the investigated compounds: Gram-positive bacteria (Bacillus subtilis ATCC 19659, Bacillus cereus ATCC 10876 and Sarcina lutea), Gram-negative bacteria (Pseudomonas fluorescens ATCC 13525); yeasts (Rhodotorula glutinis, Candida mycoderma and Saccharomyces cerevisiae) and moulds (Aspergillus niger, Geotrichum candidum and Fusarium graminearum). The ATCC bacterial strain were purchased from American Type Culture Collection. All wild bacterial and fungal strains were isolated from food spoilage microbiota.

The cultures of test microorganisms were maintained in medium agar slants at 4°C and used as stock cultures. Bacterial strains were grown at 37°C in PCA medium (casein peptone 5.0 g/L, yeast extract 2.5 g/L, dextrose 1.0 g/L, agar 15.0 g/L, pH 7.2) and the final concentration used for antimicrobial activity was 106 CFU/mL. Yeasts were grown at 25°C in MEA medium (maltose 12.75 g/L, peptone 0.78 g/L, dextin 2.75 g/L, agar 15.0 g/L, glycerol 2.55 g/L, pH 4.7) and the final concentration of 106 CFU/mL was obtained by viable counts serial dilutions. Spore suspension was obtained from the stock culture in a final concentration of 1010 spores/mL.
The qualitative evaluation of the inhibitory potential of the investigated compounds was tested by the agar diffusion test. The diffusion method involves inoculation of high cell concentrations of the test microorganisms on specific agar culture medium, at 37°C, in sterile Petri’s plates. After homogenization and solidification of the medium, on the surface plate, sterile filter paper discs (θ = 19 mm) were placed, coated (equal time, 10 min) with aqueous solutions (5 mg/mL) of the tested chemicals. The blank was a disc soaked in distilled water. The plates were incubated at optimal conditions for test culture growth (at 37°C, 48 h for bacteria, and at 25°C, for 3-5 days, for yeasts and moulds). The evaluation of microbiostatic or microbicidal effect of the studied chemical compounds was made by measuring at every 24 h, the inhibition zone diameter (DIz ≥ mm) and by checking some morphological characteristics of colonies, i.e. pigmentation, sporulation intensity.

A product is considered active if the difference between the inhibition zones of this product and that of the blank is at least of 2 mm. Considering the diameter of the tests paper discs (19 mm), the following classification of the chemical compounds activity was proposed, depending on the dimensions of the inhibition zones:

- with low inhibitory effect, DIz = 20 mm;
- with medium inhibitory effect, DIz = 20-50 mm;
- with strong inhibitory effect, DIz ≥ 50 mm.

The quantitative effect of the substances with the higher inhibitory potential of cells growth was determined in vitro, by bacterial cultivation in stationary conditions, in liquid nutrient broth medium, on the basis of the minimum inhibitory concentration (MIC) values. The most sensible microorganisms were used for quantitative evaluation. Serial dilutions (5, 2.5, 1, 0.5 and 0.25 mg chemical compound/mL medium) were prepared from stock solutions (5 mg/mL). 0.5 mL of each standardized bacterial suspension was added to an equal volume of each chemical compound dilution (excluding the sterility control). After incubation for 24 h ± 1 h at 37°C, the turbidity of the cultures associated with the veil or derma formation at the medium surface was visually assessed. The microorganism growth was monitored by optical density determination (OD600). The tests were performed simultaneously on negative controls (only medium), growth controls (medium + test microorganism) and sterility controls (medium + chemical compounds). The lowest concentration of antimicrobial agent, that inhibits the development of visible growth after 24 h of incubation at 37°C, was taken as the minimum inhibitory concentration.

All the experiments were performed in triplicate.

Results and discussions

Synthesis

The synthesis of the asymmetric diquaternary salts 3a-d has been carried out through a two step alkylation of 1,2bis(4-pyridyl)ethane (scheme 1), after a method previously developed by for the synthesis of some 4,4'-bipyridinium asymmetric diquaternary salts [27]. Thus the asymmetric diquaternary salts 3a-d were prepared by alkylation of N-methyl-1,2-bis(4-pyridinium)ethanemethiodide 1, which in turn was prepared by controlled mono-methylation of 1,2-bis(4-pyridyl)ethane with methyl iodide. The iodo alkylation reagents 2a-d (iodo aceto phenones) were prepared from the commercial bromine or chlorine derivatives following the methods described in the literature [28, 29]. The diquaternary salts 3a-d were thus obtained in good yields (51-70%).

The structure of synthesised compounds has been assigned on the basis of IR, 1H NMR, 13C NMR, MS and elemental analysis, whereas its purity was confirmed by HPLC.

The molecular structures of iodo-acetophenone derivatives 2a-d were confirmed by 1H NMR analysis, and are in concordance with the literature.

The IR spectrum of the bis-pyridinium salts 1 and 3a-d show characteristic bands in the following range: 3032-3008 cm⁻¹ (νCH=C=), 2960-2872 cm⁻¹ (νCH₂), 1691-1702 cm⁻¹ (νC=O), 1640-1638 cm⁻¹ (νC=N), 1529 and 1345 cm⁻¹ (νNO₂), 1246 and 1032 cm⁻¹ (νC-O-C) and 1102 - 988 cm⁻¹ (C-C₂ₐ₂ₘᵢₙ).

The molecular structures of 1 and 3a-d compounds were further confirmed by NMR analysis. In 1H NMR spectra the presence of a sharp singlet at 4.32 ppm confirms the presence of the N+-CH₃ group. The down field shift of the N+-CH₃ is due to the inductive effect of the quaternary nitrogen at CH₃. The quaternization of pyridine nitrogen are sustained by the shift of pyridine ring proton signals to low fields due to the shield effect of quaternary nitrogen. Thus the four protons neighbor with quaternized nitrogen give doublets signals at 8.90-8.84 ppm coupled (J~6.4-6.8 Hz) with the other four protons of pyridine rings whose doublets signals can be found at higher fields due to the shield effect of quaternary nitrogen. The characteristic singlet peaks at 6.30-6.48 ppm, for 3a-d salts, can be attributed to CH, close to the cationic nitrogen, whereas for all compounds the peak centered at 3.41-3.44 ppm is due to the bridging protons from phenyl ring. The IR spectrum of the bis-pyridinium salts 1 and 3a-d show characteristic bands in the following range: 3032-3008 cm⁻¹ (νCH=C=), 2960-2872 cm⁻¹ (νCH₂), 1691-1702 cm⁻¹ (νC=O), 1640-1638 cm⁻¹ (νC=N), 1529 and 1345 cm⁻¹ (νNO₂), 1246 and 1032 cm⁻¹ (νC-O-C) and 1102 - 988 cm⁻¹ (C-C₂ₐ₂ₘᵢₙ).

The IR spectrum of the bis-pyridinium salts 1 and 3a-d show characteristic bands in the following range: 3032-3008 cm⁻¹ (νCH=C=), 2960-2872 cm⁻¹ (νCH₂), 1691-1702 cm⁻¹ (νC=O), 1640-1638 cm⁻¹ (νC=N), 1529 and 1345 cm⁻¹ (νNO₂), 1246 and 1032 cm⁻¹ (νC-O-C) and 1102 - 988 cm⁻¹ (C-C₂ₐ₂ₘᵢₙ).
Antimicrobial activity

The results obtained through the diffusion method, after 24 h of cultivation are presented in table 1. The antimicrobial activity results showed that these newly bis-pyridinium asymmetric diquaternary salts exhibited interesting antibacterial activities; all compounds being active against at least one of the tested strains, with medium or strong inhibitory effect. The compound 3d presents the largest antimicrobial inhibition spectrum.

The tested compounds are more effective against bacteria than against yeasts or moulds. They proved to be active both on Gram-positive and Gram-negative bacteria, very interesting being the spectacular bactericide effect of some compounds (3c, 3d) against Pseudomonas Fluorescens (DIZ = 71–75 mm) tested strain. Compound 3a is the only one that not inhibits any bacterial strain.

The inhibitory effect on the yeasts is moderate, the salt 3d being the only compound that partially inhibits the growth of Rhodotorula glutinis (DIZ = 23 mm), compounds 3a and 3d inhibiting the growth of Candida mycoderma species (DIZ =22-33 mm) while 3d salt is the only inhibitor to the S. cerevisiae strain (DIZ=25 mm).

The inhibitory effect on moulds is very low, the salt 3d being the only compound with moderate activity against all tested mould strains (DIZ = 21-25 mm).

Regarding the results obtained by diffusion method, the quantitative evaluation tests were performed only on the bacterial strains and using the most active compounds for each tested strain. The cultures' growth for the Bacillus subtilis and Pseudomonas fluorescens strains was evaluated by the increasing of the turbidity associated with a veil formation at the culture surface. The turbidity was spectrophotometrically evaluated by measuring the optical density of the cultures comparatively with a sterility sample (medium + chemical compound). Minimum inhibitory concentration (MIC) represents the lowest concentration of compound at which the microorganism tested does not show visible growth.

The obtained results show that the highest activity of the tested diquaternary salts is against Bacillus subtilis strain, its growth being completely inhibited by the diquaternary salt 3d with MIC of 0.5 mg/mL. For Pseudomonas fluorescens strain, the activity of tested compounds (3c and 3d) is lower (MIC=5mg/mL).

Regarding the relations structure-activity, we can observe that the antimicrobial activity is quasi-general and none influenced by the nature of the R substitutes. The substitute nature in the phenyl ring doesn’t have a decisive influence on the biological activity, influencing mostly the selectivity. The biological activity of the tested compounds could be explained by their ionic structure, being influenced by their water solubility too. The difference between the observed antimicrobial activities is probably due to molecular hydrophobicity, absorbability, and the electron density of the ammonium nitrogen atom.

Thermogravimetric analysis

The thermal stability of asymmetric diquaternary salts 3a-d was investigated through a thermogravimetric analysis, which informs about the temperature range where the investigated compounds may be used and stored.

The decomposition temperature (T_{dec}) reported in table 2 indicates approximately when the salts start to degrade. It has been observed a not-negligible dependence on the substituent nature, i.e. the replacement in R of a H by a OCH₃ or NO₂, yields a significant increase of both decomposition and melting temperatures (endothermic peak).

The salts decomposition temperatures fall in the range 205-250°C, suggesting a high stability of these molecules (fig. 1). For 3a, 3c and 3d compounds a progressive decomposition may be observed, while for salt 3b the melting process is accompanied by a rapid decomposition followed by a direct evaporation. The decomposition is likely due to the compounds quaternary ammonium structures, the first stage being a de-alkylation reaction, with the loss of the acetophenone moiety, followed by a polymerization process, before degrading into smaller components.

**Table 1**

<table>
<thead>
<tr>
<th>Tested comp.</th>
<th>Microorganisms /DIZ (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacillus subtilis</td>
</tr>
<tr>
<td>H₂O</td>
<td>0</td>
</tr>
<tr>
<td>3a</td>
<td>0</td>
</tr>
<tr>
<td>3b</td>
<td>0</td>
</tr>
<tr>
<td>3c</td>
<td>30.33±0.57</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mp (°C)</th>
<th>T_{dec} (°C)</th>
<th>ΔH (J/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>210-211</td>
<td>205</td>
<td>143.82</td>
</tr>
<tr>
<td>3b</td>
<td>208-209</td>
<td>205</td>
<td>64.93</td>
</tr>
<tr>
<td>3c</td>
<td>238-239</td>
<td>235</td>
<td>156.41</td>
</tr>
<tr>
<td>3d</td>
<td>255-256</td>
<td>250</td>
<td>159.80</td>
</tr>
</tbody>
</table>

*T_{dec} = onset of decomposition temperature*
Conclusions

We report here the efficient synthesis of four new asymmetric diquaternary salt derived from 1,2-bis(4-pyridyl)ethane, by the quaternisation of nitrogen atom with reactive halides.

Present study shows that the new synthesized compounds present interest to be antimicrobial agents in order to produce disinfectants materials. Their inhibitory effect against yeasts and moulds are very low, comparatively with the antibacterial activity against bacteria.

TGA analysis was performed for all the asymmetric synthesized diquaternary bis-pyridinium salts, indicating the thermal stability of them up to around 205-250°C. This indicates a good stability of compounds which facilitate their use and storage.

Acknowledgements: This work has benefited from financial support through the 2010 POSDRU/89/1.5/S/52432 project, ORGANIZING THE NATIONAL INTEREST POSTDOCTORAL SCHOOL OF APPLIED BIOTECHNOLOGIES WITH IMPACT ON ROMANIAN BIOECONOMY, project co-financed by the European Social Fund through the Sectorial Operational Programme Human Resources Development 2007-2013.

References


Manuscript received: 14.03.2012